REMARKS

Applicants have amended the specification such that a statement in the summary is consistent with the clinical data presented in Table 1. No new matter has been introduced by the present amendment.

Reconsideration of the application, as amended, is requested in view of the following remarks:

Rejection under 35 U.S.C. § 103(a)

Claims 1-10 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over Sager et al. (US Patent No. 5,470,970; "970") in view of Ding et al. (Proceedings of the American Association of Cancer Research, 1996, vol. 37, page A627; "Ding et al.") and either Gregory et al. (US Patent No. 5,932, 210; "210") or Hung et al. (US Patent No. 6,197,754; "754"). More specifically, the Examiner maintained that:

> "Sager et al teach that maspin functions as a tumor suppressor gene in breast cancer. Ding et al teach that maspin gene expression is found in breast epithelial cells and in squamous cell carcinomas of the esophagus and tongue. Either Gregory et al (column 21, lines 64-67) or Hung et al teach that the presence of a tumor suppressor gene product (column 12, lines 12-14) is correlated with increased survival time. Thus the prior art teaches that maspin is a tumor suppressor gene found in squamous cell carcinoma, and the presence of tumor suppressor gene is indicative of increased survival time. Thus one of skill in the art would conclude that the expression of the maspin tumor suppressor gene in a sample of squamous cell carcinoma would indicate a relatively high probability of survival in a patient in contrast to samples exhibiting a lack of expression of said gene." See the Office Action, part 5, pages 2 and 3.

Applicants disagree. Claims 1 and 6, the two independent claims, will be discussed first. Both claims are drawn to methods of predicting a relative probability of survival for a subject with squamous cell carcinoma according to the expression level of the maspin gene. See the specification, e.g., page 3, lines 7-11 and page 10, lines 4-9. None of the prior art references cited by the Examiner, alone or in combination, discloses such a prediction method.

As correctly pointed out by the Examiner, '970 teaches that maspin functions as a tumor suppressor gene in breast cancer and Ding et al. teaches that maspin is expressed in squamous

cell carcinomas. However, neither of them suggests that the level of maspin gene expression can be used to predict the relative probability of survival for a subject with squamous cell carcinoma. '210 and '754, on the other hand, disclose that treating a mouse with a specific tumor suppressor gene (p53 in '210 and E1A in '754) results in longer survival time. See, e.g., '210, Example IV at column 43; and '754, column 22, lines 21-25. Neither suggests that the p53 gene or the E1A gene can be used as a prognostic marker for predicting the survival time of a mouse, let alone indicating that other tumor suppressor genes (e.g., maspin) can be used as such prognostic markers. Thus, one would not have been motivated by the cited references to come up with the claimed prognostic methods.

Further, even if one would conclude, based on the teachings of '210 and '754, that the p53 gene or the E1A gene can be used a prognostic marker, one still would not have been motivated to apply it to the maspin gene. It is well known in the art that tumor suppressor genes function through different pathways and have different effects on tumorigenesis. One tumor suppressor gene (e.g., p53 or E1A) being associated with the survival time of a subject with a particular type of cancer does not necessarily indicate that another tumor suppressor gene (e.g., maspin) being associated with the survival time of a subject with the same or another type of cancer. Moreover, even if one might have been motivated to use maspin as a prognostic marker (which Applicants do not concede), there would not have been reasonable expectation of success for using such a marker to predict a relative probability of survival for a subject with squamous cell carcinoma. Expression of a tumor suppressor gene in cancer tissues does not imply that the tumor suppressor gene is useful for making prognosis of the cancer. For example, p53 has been found to be expressed in breast cancer, yet the expression of p53 does not correlate with the survival rate of breast cancer patients. See, e.g., Mourao et al., 2001, Braz J Med Biol Res 34(7): 887-94, a copy of which is attached hereto as "Exhibit A." Therefore, without the teaching of the present specification, one would not have predicted with a reasonable expectation of success that maspin can be used for predicting a relative probability of survival for a subject with squamous cell carcinoma.

For the reasons set forth above, claims 1 and 6 are patentably distinguishable over the cited art. So are claims 2-5 dependent from claim 1 and claims 7-10 dependent from claim 6.

CONCLUSION

Applicants submit that the ground for rejection asserted by the Examiner has been overcome, and that claims 1-10, as pending, define subject matter that is non-obvious and thus patentable. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Attached is a marked-up version of the changes being made by the current amendment.

Enclosed is a $55 check for the Petition for Extension of Time fee. Please apply any other charges to Deposit Account No. 06-1050, referencing 12005-002001.

Respectfully submitted,

Date: 8-9-02

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Version with markings to show changes made

In the specification:

The bridging paragraph between pages 1 and 2 has been replaced with the following rewritten paragraph:

The invention also features a method of determining whether a subject (e.g., a human patient) with squamous cell carcinoma has a lymph node containing cancerous cells by determining a level of maspin gene expression in a biological sample from a subject with squamous cell carcinoma; and comparing the level with a threshold level of maspin gene expression. A level of maspin gene expression in the biological sample above a threshold level indicates that the subject [has] does not have a lymph node containing cancerous cells, and a level of maspin gene expression in the biological sample below a threshold level indicates that the subject [does not have] has a lymph node containing cancerous cells.